REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Claims 1-6 are rejected under 35 USC 112, first paragraph, on the basis that claims are not enabled by the disclosure based upon the breadth of the terms "humectants" and "crosslinking agents".

Claim 1 has been amended to recite the preferred humectants and crosslinking agents. These amendments are supported in the specification at page 8, lines 6-13 and page 9, lines 7-17.

In view of the foregoing amendments, this ground of rejection is deemed to be overcome.

Claims 1-6 are rejected under 35 USC 112, second paragraph, for the reasons set forth in item 5 on page 3 of the Action.

These grounds of rejection are deemed to be overcome in view of the foregoing amendments.

Claims 1-6 are rejected under 35 USC 103 as being unpatentable over USP 5,725,874 or USP 5,173,302 each standing by itself or in combination with USP 6,455,066. This ground of rejection is respectfully traversed.

It is recognized by the Examiner that the references do not teach the combination of both an analgesic and an anesthetic in an external skin patch, according to the claimed invention.

The Examiner mentions that it is within the skill in the art to combine two known drugs having the same effect in order to have a synergistic effect. However, an analgesic and an anesthetic have different effects from each other. An analgesic is effective for anti-inflammatory effects. On the other hand, an anesthetic is effective for pain sensation suppressing effects. Therefore, the nonsteroidal antiphlogistic analgesic agent and the local anesthetic agent have different action mechanisms from each other. Hence the Examiner's reasoning is mistaken.

An external preparation of a nonsteroidal antiphlogistic analgesic agent alone is not effective for the remedy of composite pains caused by pinching of nerve, nerve stimulus, bleeding, edema and so on which are accompanied by inflammation, such as chronic rheumatism, arthrosis

deformans or low back pain. Likewise, an external preparation of a local anesthetic alone is ineffective.

Such ineffectiveness is attributable to the following reasons. Namely, the nonsteroidal antiphlogistic agent and the local anesthetic agent have different action mechanisms as mentioned above, and these external preparations for suppressing pains are locally-administrated remedies. Thus, each of these agents, when used alone, cannot be an effective remedy against composite pains of the kind described above.

On the other hand, a local administration of the mixture of both an analgesic and an anesthetic of the present invention can suppress the composite pains. The present invention is based on a finding that a highly effective remedy for the diseases of the kind described above can be achieved by local administration of the mixture of a nonsteroidal antiphlogistic analgesic agent and a local anesthetic agent.

Thus, the synergistic effect obtained by the combination of both an analgesic and an anesthetic is not merely the combination of the known effect of analgesic and the known effect of anesthetic. The composite pains which are not suppressed by an analgesic nor by an anesthetic alone, can be suppressed by the mixture of an analgesic and an anesthetic of the present invention. The preparation of the present invention is effective for treating symptoms which are known to be ineffective by analgesic and anesthetic when used alone. Accordingly, it would have not been obvious to one having ordinary skill in the art to predict the synergistic effect of the present invention by combining an analgesic with an anesthetic to achieve the present invention.

The Examiner also alleges that motivation to combine an analgesic and anesthetic in a reservoir would arise from the general knowledge in the art that analgesics and anesthetics both act in synergism to relieve pain. However, the it is respectfully submitted that there is no such general knowledge in the art, and the Examiner is requested to support such position with a prior art publication.

The Examiner also relies on the '066 U.S. patent. Applicants intend to remove such reference as prior art under 35 USC 119. An English translation of Applicants' Japanese priority

application is submitted herewith, which shows the claimed subject matter is fully supported by the priority application. A verified English translation will be submitted in due course.

In summary, it is respectfully submitted that a proper *prima facie* case of obviousness has not been established. To establish a *prima facie* case of obviousness, there must be some suggestion or motivation in the prior art to modify the teachings of the reference, or to combine the reference teachings. The initial burden is on the Examiner to provide some suggestion of the desirability of doing what the inventor has done. To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention, or the Examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the cited references. Here, there is no teaching or suggestion in the prior art to motivate the artisan along the lines of the claimed invention, nor is there any convincing line of reasoning to do so.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made**."

Accordingly, reconsideration and allowance is respectfully solicited.

Respectfully submitted,

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February 19, 2003

CLAIMS

(Amended)

1. An external skin patch, comprising a substrate and a drug reservoir layer coated on the substrate, in which the drug reservoir layer comprises ~~a drug-containing base containing~~ (1) an adhesive gel base comprises which ~~contains~~ a water soluble polymeric material, a crosslinking agent, water and together with (2) medicinal components comprising a humectant as essential components, ~~and~~ a local anesthetic and a nonsteroidal antiphlogistic analgesic agent ~~as medicinal components~~, wherein the crosslinking agent is selected from the group consisting of aluminum compounds, and

(Amended)

2. An external skin patch according to claim 1, in which the local anesthetic comprises one or more ~~kinds of~~ compounds selected from the group consisting of tetracaine, procaine, dibucaine, lidocaine, benzocaine, xylocaine, and pharmaceutically acceptable salts thereof.

3. An external skin patch according to claim 1 or claim 2, in which the nonsteroidal antiphlogistic analgesic agent comprises one or more (kinds of) compounds selected from the group consisting of indomethacin, ketoprofen, piroxicam, felbinac, bufexamac, suprofen, flurbiprofen, diclofenac, ibuprofen and pharmaceutically acceptable salts thereof.

4. An external skin patch according (to any of) claims 1 to 3, in which the drug-containing base contains the local anesthetic is present in an amount of 0.1 - 50 % by weight.

5. An external skin patch according to any of claims 1 to 4, in which the drug-containing base contains the

wherein the ~~humectant~~ is selected from the group consisting of polyhydric alcohols, saccharides and superabsorbent resins.

Version with Markings to Show Changes Made

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of :

Keiko YAMASAKI et al. : **Attn: BOX PCT**

Serial No. NEW : **Docket No. 2001_1026A**

Filed August 24, 2001 :

EXTERNAL SKIN PATCH
[Corresponding to PCT/JP00/07451
Filed October 25, 2000]

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents,
Washington, DC 20231

Sir:

Prior to calculating the filing fee, please amend the above-identified application as follows:

IN THE SPECIFICATION

Page 1, immediately after the title, please insert:

This application is a 371 of PCT/JP00/07451 filed October 25, 2000.

IN THE CLAIMS

Please amend the claims as follows:

3. (Twice Amended) An external skin patch according to claim 1, in which the nonsteroidal antiphlogistic analgesic agent comprises one or more ~~kinds of~~ compounds selected from the group consisting of indomethacin, ketoprofen, piroxicam, felbinac, bufexamac, suprofen, flurbiprofen, diclofenac, ibuprofen and pharmaceutically acceptable salts thereof.

Twice wherein

4. (Amended) An external skin patch according to claim 1, ~~in which the drug-containing base contains~~ the local anesthetic is present in an amount of 0.1 - 50% by weight.

Twice wherein

5. (Amended) An external skin patch according to claim 1, ~~in which the drug-containing base contains~~ the nonsteroidal antiphlogistic analgesic agent is present in an amount of 0.05 - 10% by weight.

Kindly add the following new claim:

(Amended)

6. An external skin patch according to claim 1, in which the local anesthetic comprises one or more ~~kinds of~~ compounds selected from the group consisting of lidocaine and pharmaceutically acceptable salts thereof, and the nonsteroidal antiphlogistic analgesic agent comprises one or more ~~kinds of~~ compounds selected from the group consisting of indomethacin, felbinac, diclofenac and pharmaceutically acceptable salts thereof.